Firing patterns in model networks of hippocampal persistent firing neurons

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Motivation

- Persistent firing has long been thought to be the neural mechanism underlying short-term memory encoding and storage [1]
- Intrinsic neural mechanisms [2] can sustain persistent firing in hippocampal CA1 neurons [3] in the absence of external stimulation
- We analyse the dynamics of networks of persistent firing hippocampal neurons
- We hypothesise that these circuits could contribute to the **emergence of theta oscillations in the hippocampus**

Neuron Model

- Neuron Model [4]:

$$C_m \cdot \frac{\mathrm{d}V_m}{\mathrm{d}t} = -I_{Leak} - I_K - I_{Na} - I_M - I_{Ca} - I_{CAN} - I_{Syn} + I_{Stim}$$

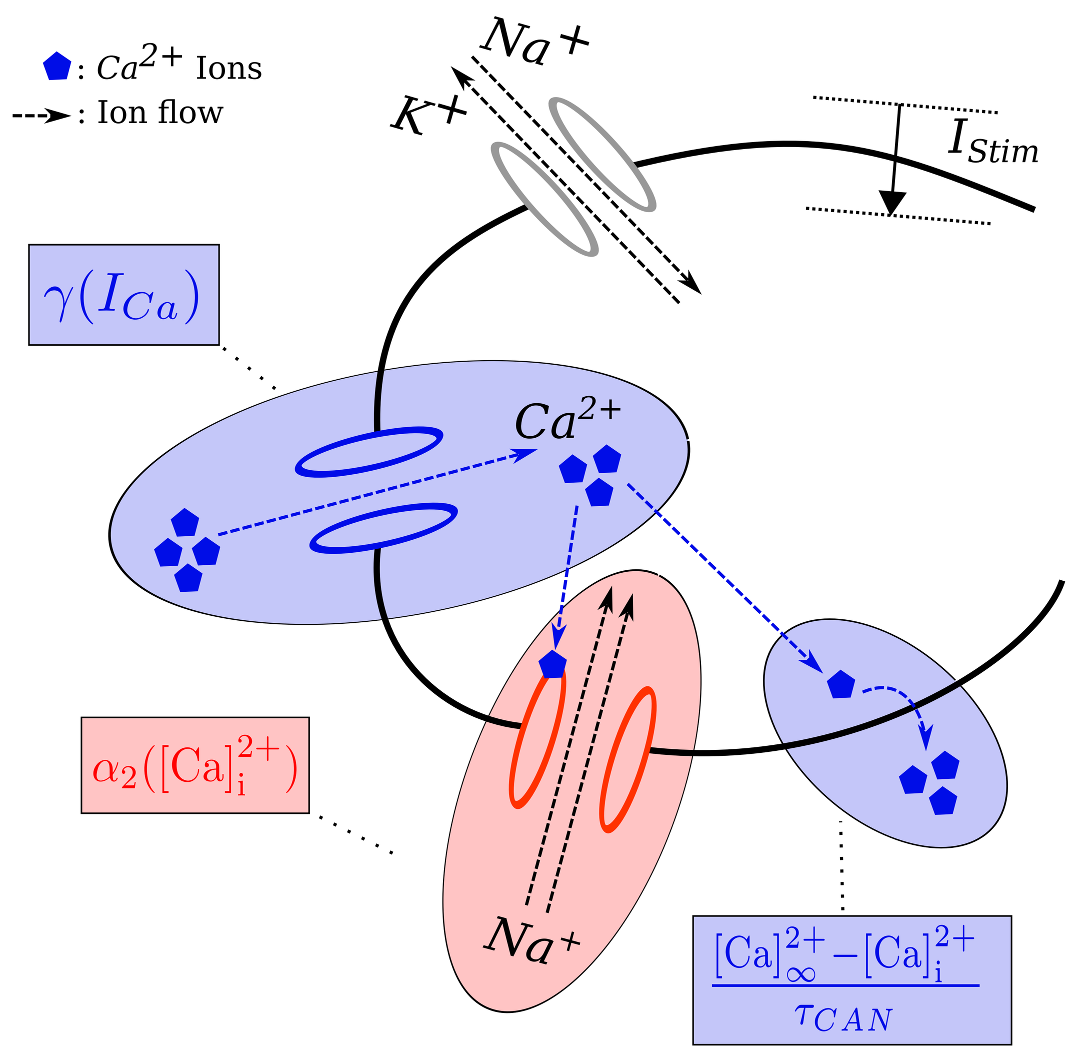
- Hodgkin-Huxley and M Currents:

$$I_{Leak} = f(V_m) \qquad I_K = f(V_m, n^4) \qquad I_{Na} = f(V_m, m^3, h) \qquad I_M = f(V_m, m)$$

- Excitatory Postsynaptic Current:

$$I_{Syn} = -g_E \cdot (V_m - E_E) \qquad \frac{\mathrm{d}g_E}{\mathrm{d}t} = -\frac{g_E}{\tau_E} \qquad g_E \leftarrow g_E + w_{ee} \qquad E_E = 0\,mV \qquad \tau_E = 5\,ms$$

Calcium Dynamics



Schematic of the Calcium dynamics (influx and efflux) and the activated CAN current. Ca^{2+} ions (blue) enter the cell membrane, and bind on CAN receptors (red) causing them to open and permeate K^+ and Na^+ ions.

- The Calcium Dynamics:

$$I_{Ca} = f(V_m, m^2, h) \qquad \frac{\mathrm{d}[\mathrm{Ca}]_i^{2+}}{\mathrm{d}t} = \gamma(I_{Ca}) + \frac{[\mathrm{Ca}]_\infty^{2+} - [\mathrm{Ca}]_i^{2+}}{\tau_{Ca}} \qquad \gamma(I_{Ca}) = \frac{-10^4 \cdot I_{Ca}}{area \cdot 2 \cdot F \cdot depth}$$

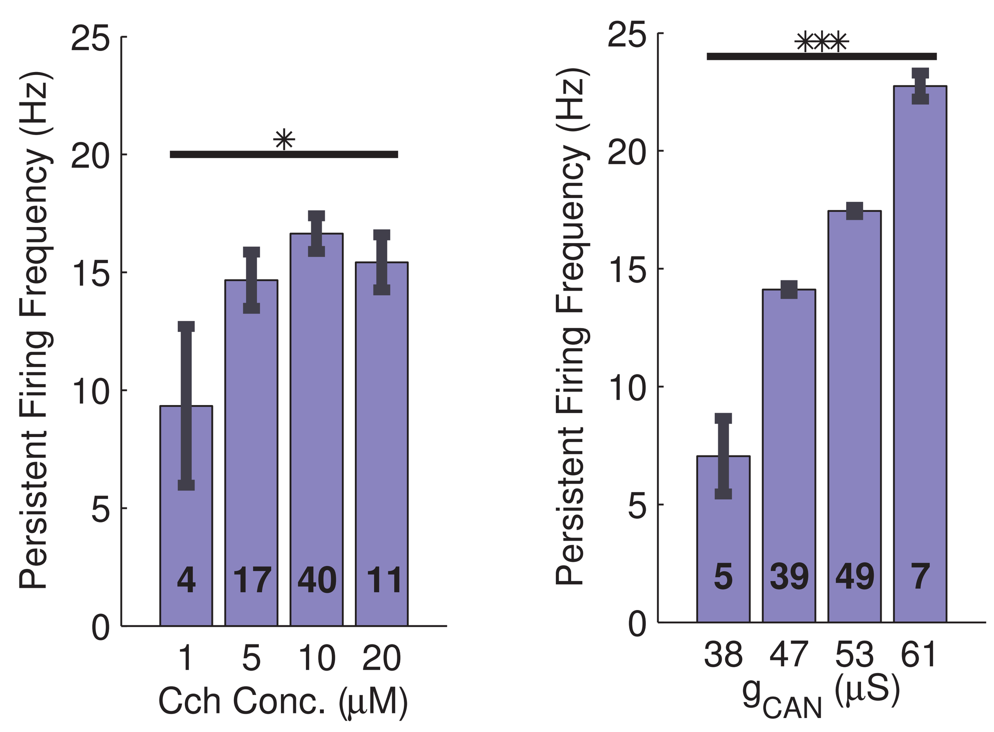
$$[\mathrm{Ca}]_\infty^{2+} = 24\,\mu M \qquad \tau_{Ca} = 200\,ms$$

- The CAN Current:

$$I_{CAN} = f(V_m, m^2) \qquad \frac{\mathrm{d}m}{\mathrm{d}t} = \alpha_m \cdot (1-m) - (\beta_m \cdot m) \qquad \alpha_m = \alpha_2([\mathrm{Ca}]_i^{2+}) \cdot T \qquad \beta_m = \beta_{CAN} \cdot T$$

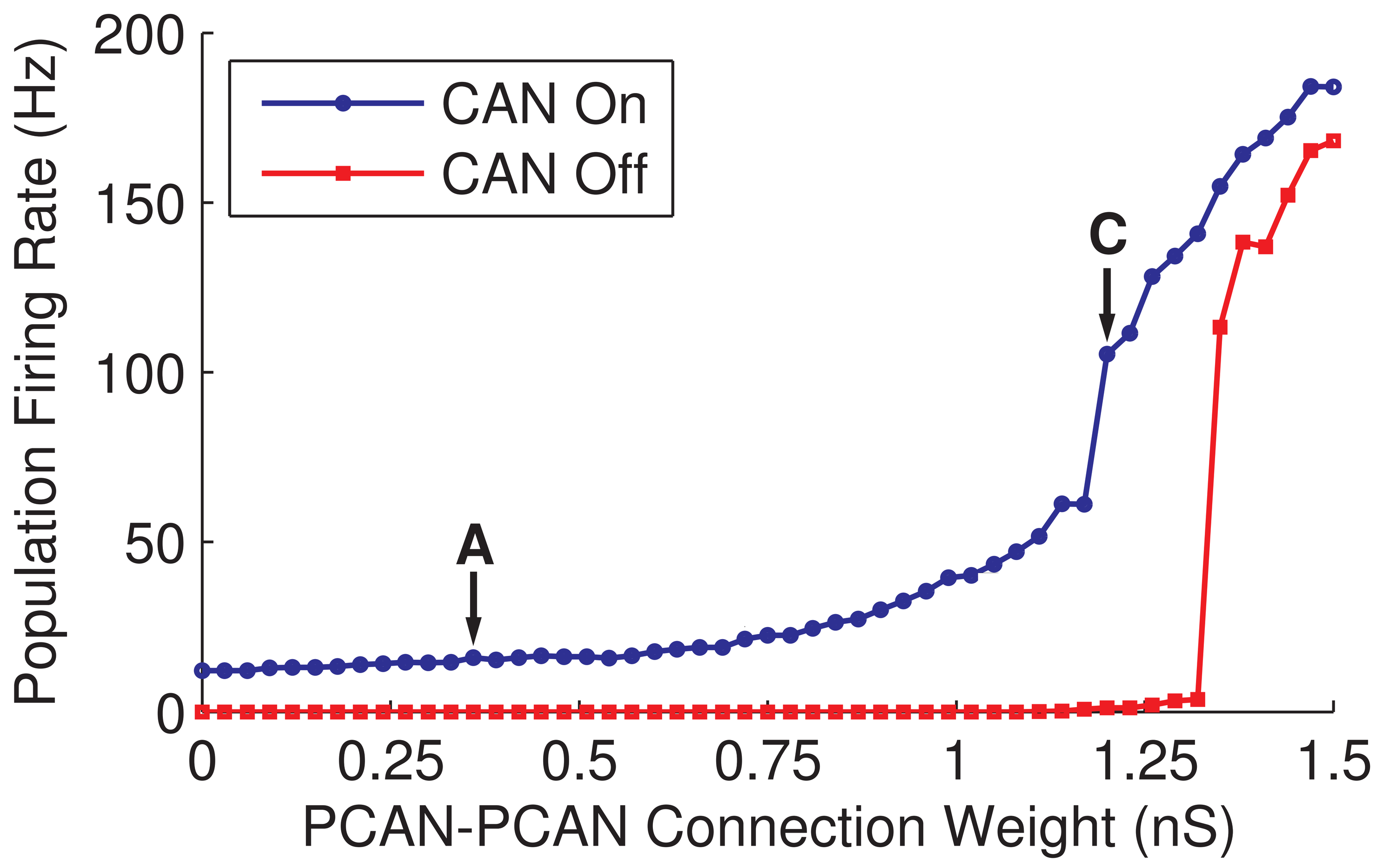
$$\alpha_2([\mathrm{Ca}]_i^{2+}) = \beta_{CAN} \cdot \left(\frac{[\mathrm{Ca}]_i^{2+}}{[\mathrm{Ca}]_c^{2+}}\right)^2 \qquad \beta_{CAN} = 0.2\,s^{-1} \qquad [\mathrm{Ca}]_c^{2+} = 50\,\mu M$$

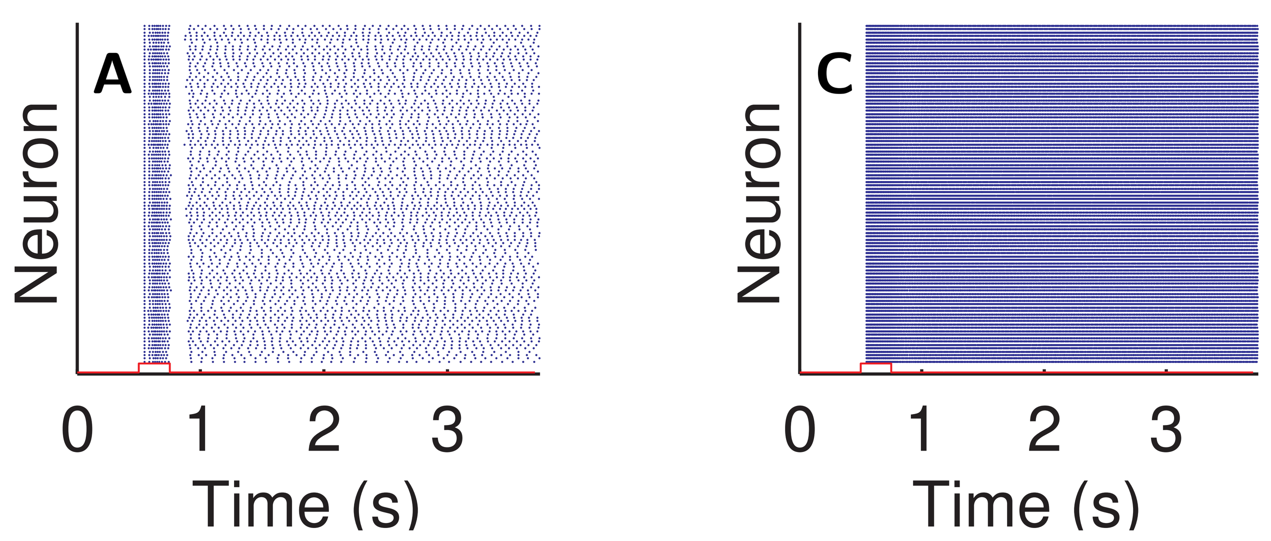
Fitting Model to In-Vitro Data



The persistent firing frequency is modulated by the activation of CAN receptors in the model (right) in accordance with *in vitro* recordings [3] (left).

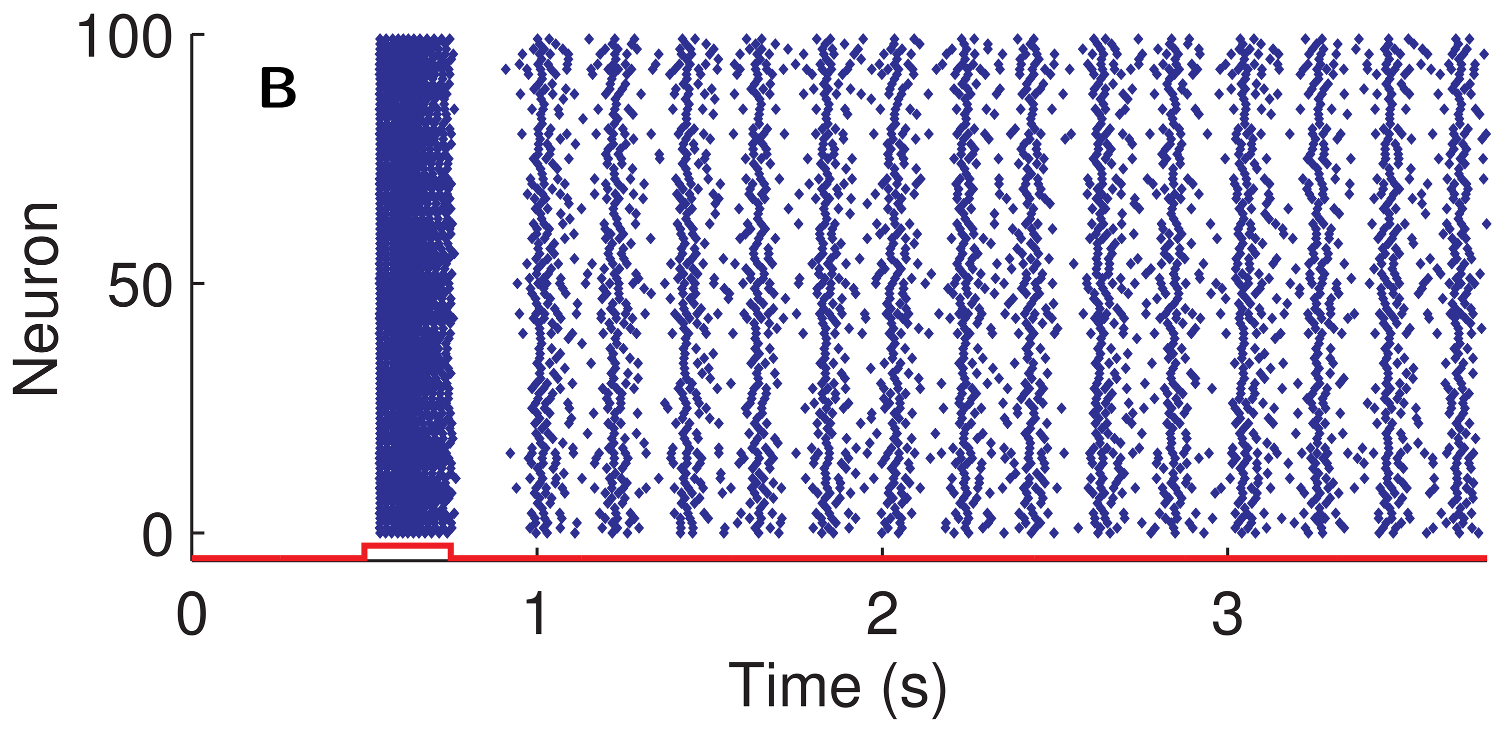
Results – Network Firing Regimes

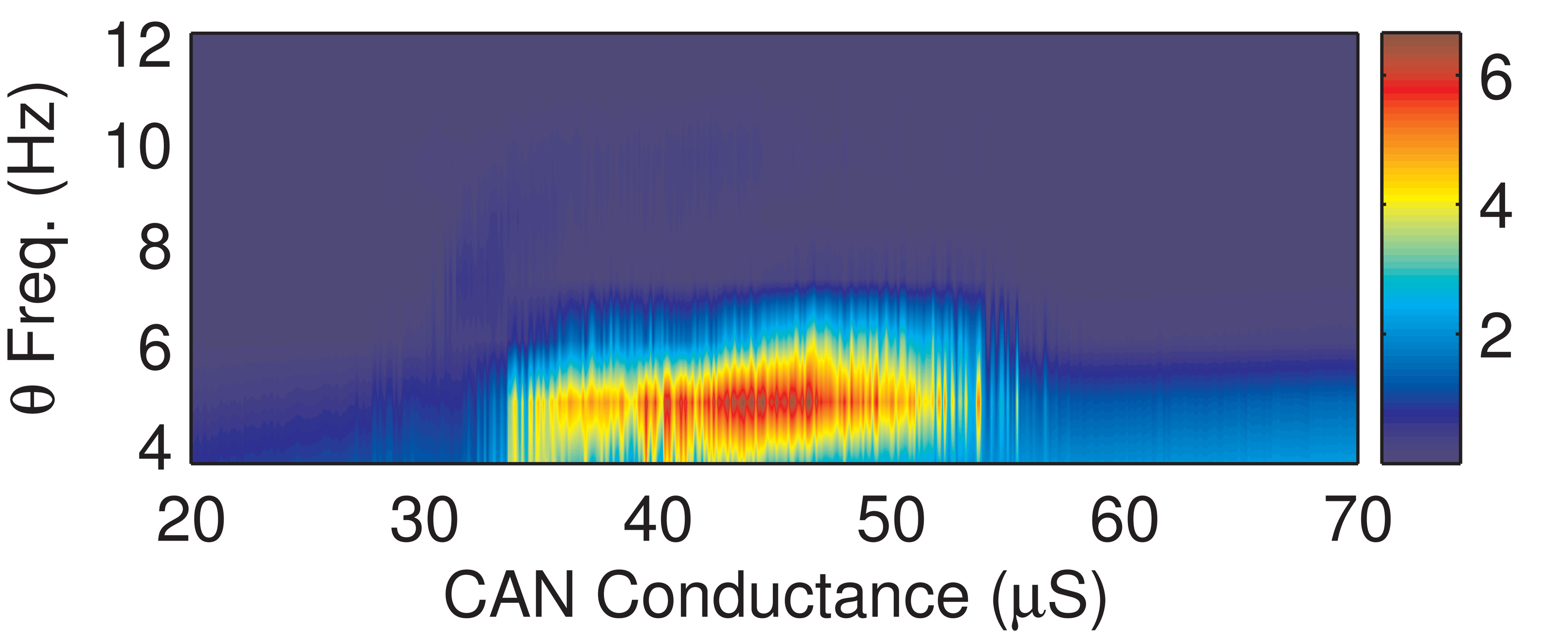




The CAN current activation allows a 100-cell network to display persistent firing in biologically plausible frequency bands. Conversely, a pyramidal network without CAN current (bottom line) does not display such a rich firing regime.

Results – CAN-Mediated Theta Oscillations





The interaction between CAN-mediated persistent firing and synaptic activity allow for the emergence of self-sustained synchronous theta oscillations in the CAN pyramidal network.

Conclusion

- Networks of CAN-equipped neurons display a rich array of firing regimes
- Self-sustained theta oscillations emerge from the interaction between CAN-mediated persistent firing and synaptic activity

References

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